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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,364	07/19/2000	Nathaniel Heintz	600-1192N2	2192

7590

09/25/2003

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EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

21

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/619,364	HEINTZ ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 July 2003.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 and 20-48 is/are pending in the application.
- 4a) Of the above claim(s) 1-14 and 33-47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-17, 20, 27 and 48 is/are rejected.
- 7) ☒ Claim(s) 18, 21-26 and 28-32 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

Receipt is acknowledged of an amendment, filed 7/11/03 as Paper No. 20, in which claim 27 was amended to clarify its content. Receipt is also acknowledged of a Terminal Disclaimer (TD) over U.S. Patent No. 6,485,912 submitted 7/11/03 as Paper No. 19. This TD is proper and has been entered into the file. Claims 1-18, 20-48 are pending in the instant application, with claims 1-14, 33-47 withdrawn from consideration as being withdrawn from consideration as being directed to nonelected inventions.

### ***Response to Amendment***

The TD submitted as Paper No. 19 obviates the outstanding Obviousness Double Patenting rejection made in the previous office action (Paper No. 18 mailed 4/18/03). The outstanding rejection of claim 27 for indefiniteness under 35 U.S.C. 112 2<sup>nd</sup> paragraph is maintained for reasons outlined below. This action is not final, as new grounds for rejecting claims are presented below that were not necessitated by applicants' amendment of the claims in Paper No. 20.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

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the invention. **This rejection is maintained for reasons of record in Paper No. 18, mailed 4/18/03 and repeated below.**

Claim 27 recites the limitation "wherein the two homologous nucleotide sequences are IRESEGFP". The term "IRESEGFP" appears to refer to an internal ribosome entry site (IRES) sequence operatively linked to a nucleotide sequence encoding an enhanced green fluorescence protein (EGFP). The exact nucleotide sequence encompassed by this term is not described in the instant application and does not appear to be a consensus sequence known in the art.

#### ***Response to Arguments***

Applicant's arguments filed in Paper No. 20 have been fully considered but they are not persuasive. The response essentially argues: 1) the amendment of claim 27 presented in Paper No. 27 clarifies the metes and bounds of the term "IRESEGFP", and 2) there is evidence in the prior art that the sequences encoding green fluorescent proteins are known in the art (e.g. U.S. Patent Nos. 5,491,084 and 5,777,079).

The amendment of claim 27 and the cited patents do not address the issue of the exact nucleic acid sequence corresponding to the term IRESEGFP. The term "IRESEGFP" is used in the claim and specification to refer to a particular marker sequence. There does not appear to be any support in the specification for using the term "IRESEGFP" in a broad sense as encompassing any combination of IRES sequence and sequence encoding a green fluorescence protein. Applicants are invited to point out specific support in the specification of the use of the term "IRESEGFP" to refer to a genus of sequences comprising an IRES sequence and sequence encoding a green fluorescence protein.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-17, 20, 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-50 of U.S. Patent No. 6,143,566.

Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

The rejected claims from the instant application are directed towards a general method of selectively performing homologous recombination with a particular nucleotide sequence present on a Bacterial or Bacteriophage-Derived Artificial Chromosome (BBPAC). The methods comprise the use of a recombination-deficient host cell and a conditional replication shuttle vector, where the shuttle vector encodes a protein that mediates recombination between the particular nucleotide sequence on the BBPAC and a homologous sequence on the shuttle vector.

The claims of the '566 patent are drawn towards methods of selectively performing homologous recombination on a particular nucleotide sequence in a recombination deficient cell. The cells can be recA-. The recombinase responsible for inducing recombination can be present

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on a conditional shuttle vector and the particular nucleic acid sequence can be present on a bacterial or bacteriophage-derived artificial chromosome (BBPAC). The recombinase protein can be a "RecA-like protein", including RecA. The claims of the '566 patent are species of the broader genus claims of the instant application and necessarily make obvious the claims of the instant application.

Claims 15-17, 20, 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10, 13-30 of U.S. Patent No. 6,130,090. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

The rejected claims from the instant application are directed towards a general method of selectively performing homologous recombination with a particular nucleotide sequence present on a Bacterial or Bacteriophage-Derived Artificial Chromosome (BBPAC). The methods comprise the use of a recombination-deficient host cell and a conditional replication shuttle vector, where the shuttle vector encodes a protein that mediates recombination between the particular nucleotide sequence on the BBPAC and a homologous sequence on the shuttle vector.

The claims of the '090 patent are drawn towards methods of selectively performing homologous recombination on a particular nucleotide sequence in a recombination deficient cell in order to introduce a eukaryotic promoter exon/intron unit (PEU) into a BBPAC. The cells can be recA-. The recombinase responsible for inducing recombination can be present on a conditional shuttle vector. The recombinase protein can be a "RecA-like protein", including

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RecA. The claims of the '090 patent are species of the broader genus claims of the instant application and necessarily make obvious the claims of the instant application.

***Conclusion***

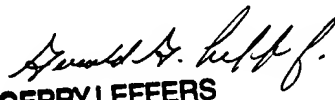
Claims 15-18, 20-32 and 48 are under consideration. Claims 15-17, 20, 27 and 48 are rejected. Claims 18, 21-26, 28-32 are objected to as being dependent upon a rejected claim, but would be allowable if rewritten as independent claims comprising each of the limitations of the claims upon which they are currently dependent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr., PhD  
Examiner  
Art Unit 1636

  
**GERRY LEFFERS**  
**PRIMARY EXAMINER**

Ggl